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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/183,566 | 10/30/98 | CONTAG | .P PXE-002P1.US |

022930 HM12/1205
HOWREY SIMON ARNOLD & WHITE LLP
BOX 34
1299 PENNSYLVANIA AVENUE NW
WASHINGTON DC 20004

| EXAMINER | |
|---|---|
| ZEMAN,R | |
| **ART UNIT** | **PAPER NUMBER** |
| 1645 | 15 |

**DATE MAILED:** 12/05/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/183,566 | Contag et al. |
| **Examiner** | **Group Art Unit** |
| Robert A. Zeman | 1645 |

☒ Responsive to communication(s) filed on *Oct 30, 1998* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *1-24* is/are pending in the application.

Of the above, claim(s) *19-24* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-18* are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

## DETAILED ACTION

### *Election/Restriction*

Applicant's election of Invention I, **without traverse**, in Paper No. 12 is acknowledged. Claims 19-24 have been withdrawn from consideration. Claims 1-18 are pending and currently under examination.

### *Claim Objections*

Claim 1 is objected to because of the following informalities: Said claim should end with a period. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the use of the phrase "which recognition activates...". It is unclear what "recognition" activates the intracellular signal transforming

domain. Nor is it clear as to what "recognition" entails? Is applicant claiming that the binding of a specific ligand to the extracellular moiety activates the intracellular signal transforming domain or is activation of said domain achieved in another manner? Additionally, the phrase "causes expression of the reporter gene to generate a reporter gene product" is confusing. Is the reporter gene product the direct result of reporter gene expression or are there intermediates? As written it is impossible to determine the metes and bounds of the claimed invention.

Claim 4 is rendered vague and indefinite by the use of the phrase "reporter gene product is bioluminescence". Bioluminescence is a physical property of compounds not a protein. Consequently it is impossible to determine the metes and bounds of the claimed invention. Substituting said term with the term "bioluminescent protein" is suggested

Claim 5 is rendered vague and indefinite by the use of the term "luciferase". Luciferase refers to a gene product (an enzyme) not a gene. Substituting said term with the term "luciferase gene" is suggested.

Claim 7 recites the limitation "intracellular signal transforming **element**" in line 1 of claim. There is insufficient antecedent basis for this limitation in the claim. All previous references are to "intracellular signal transforming **domain**".

Claim 11 is rendered vague and indefinite by the use of the phrase "or fragment thereof". It is unclear what constitutes a "fragment". What percentage of the antibody must be retained in order to constitute a fragment? What biological or immunological properties must be present? As

written it is impossible to determine the metes and bounds of the claimed invention. Substituting said phrase with the phrase "ligand-binding fragment thereof" is suggested

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Contag et al. (U.S. Patent 5,650,135, IDS-7) and Georgiou et al. (1997 Nature Biotechnology, Vol. 15, pages 29-34, IDS-7) in view of Kasahara et al. (Journal of Bacteriology, 1991 Vol. 173, No. 2, pages 6760-6765, IDS-7).

The aforementioned claims are drawn to a biodetector consisting of a signal converting element (transmembrane fusion protein) coupled to a reporter gene (luciferase) via a responsive element. Said biodetector may further comprise a bacterial cell.

Contag et al. disclose biocompatable compound consisting of an entity such as a bacterial cell and a light generating moiety such as luciferase (see column 2 lines 60-61 to column 3, lines 1-3). Contag et al further disclose that said moiety can be expressed via *in situ* synthesis in the entity (i.e. expression of a heterologous bioluminescent protein in a transformed cell or the *in situ* activatable promoter controlled expression of a bioluminescent protein. (see column 3, lines 11-14, column 4, lines 18-21 and column 7, 31-39). Contag et al. also disclose luciferase vector constructs that can be adapted for use in transforming a variety of host cells including bacteria (see column 10, 60-63). Finally, Contag et al disclose the use of antibodies and antibody fragments to confer specificity to the compound. Contag et al. differs from the claimed invention in that they do not specifically disclose the use of the phoP-phoQ operon as the regulatory system nor do they explicitly disclose the recombinant expression of the antibodies or antibody fragments on the bacterial surfaces. Kasahara et al. disclose the phoP-phoQ operon and its uses. Kasahara et al. further disclose the sequences of said operon and its use in operon fusions (See Figure 2 and page 497). Georgiou et al. disclose the methods for the recombinant expression of heterologous proteins on the surface of bacteria (both gram positive and gram negative) including scFv (see page 32-33 and Table 1). Since the use of various regulatory promoters (operons) would be known by one of skill in the art, it would have been obvious to said artisan to use the

phoP-phoQ operon disclosed by Kasahara et al. and the heterologous scFv disclosed by Georgiou et al. in order to take advantage of the increase in specificity, diversity, and ease of production of the resulting biodetector. Additionally, by varying the scFv, one could easily create a library of biodetectors (see Georgiou et al.).

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Lynette Smith, can be reached at (703)308-3909.

DONNA WORTMAN
PRIMARY EXAMINER

Robert A. Zeman

November 29, 2000